Regulation of acid base balance

When speaking about regulation of acid and base balance, we are mainly speaking about regulation of hydrogen ions concentration.

Hydrogen ions concentration, as it is for other ions, is important to be regulated because any change in it affects the enzyme system of the cells, which affects cells' functions of the body.

Normal concentration of hydrogen ions in extracellular fluid is very small compared to other ions, 0.00004 mEq/L. For this reason, this number was substituted by logarithmic scale using PH units.

PH= log 1/ [H+]

$$pH = \log \frac{1}{[H^+]} = -\log [H^+]$$

For example, the normal $[H^+]$ is 40 nEq/L (0.00000004 Eq/L). Therefore, the normal pH is

$$pH = -\log [0.00000004]$$
$$pH = 7.4$$

So concentration of hydrogen ions is inversely related to PH, when H^+ concentration increases ▲, PH decreases ▼and vice versa.

Acids and Bases:-

Acids: are substances that release hydrogen ions, example: HCL.
Bases: are substances that accept hydrogen ions, example: HCO_3^-.

There are strong and weak acids and bases,

- Strong acids: release hydrogen ions rapidly, HCL.
- Weak acids: release hydrogen ions weakly, H_2CO_3.
- Strong bases: accept hydrogen ions strongly, OH^-.
- Weak bases: accept hydrogen ions weakly, HCO_3^-.

There are three primary systems for regulation of hydrogen ions concentration (three lines of defence against hydrogen ions concentration change):

1) Chemical body fluid buffers, react within seconds.
2) Respiratory system, reacts within minutes.
3) Kidneys, reacts within hours to several days.

1st line of defence against H^+ concentration change, Chemical body fluid buffers:-

Buffer: a substance that binds reversibly with hydrogen ions.

Buffer + H+ ↔ bufferH

In acidosis reaction will be to the right, and in alkalosis reaction will be to the left.

Concerning first line of defence, chemical body fluid buffers:

1) Bicarbonate buffer system.
2) Phosphate buffer system.
3) Proteins.

<u>Bicarbonate buffer system:-</u>

$HCL + NaHCO_3 \rightarrow NaCl + H_2CO_3 \rightarrow H_2O + CO_2$

$NaOH + H_2CO_3 \rightarrow NaHCO_3 + H_2O$

Form this chemical equation, when strong acid (HCL) is added to solution it will react with $NaHCO_3$ and produce a weak acid (H_2CO_3), and strong acid will change into weak acid, so that buffer helps to decrease the change in

the H^+ concentration. Likewise, when a strong base is added to the solution it will react with H_2CO_3 and produce $NaHCO_3$, a weak base.

Components of the system are Co_2 and HCO_3.
It is the most important buffer system in the extracellular fluid.

Concerning buffer power: there are two conditions to call a buffer system a powerful one:

1. Concentration of its components is high.
2. Its PK (negative logarithm of dissociation constant) of the buffer is near the PH of the fluid.

PK of bicarbonate buffer = 6.1 and PH of ECF= 7.4, so it's not near it. And its components' concentration is not high. So it gains its power because its components can be regulated by kidneys and lungs, kidneys regulate bicarbonate and lungs regulate CO_2.

<u>Phosphate buffer system:-</u>

$HCL + Na_2HPO_4 \rightarrow NaCl + NaH_2PO_4$

$NaOH + NaH_2PO_4 \rightarrow H_2O + Na_2HPO_4$

From this equation, if we add a strong acid to the solution it will react with Na_2HPO_4 and produce NaH_2PO_4 (weak acid). If we add a strong base it will react with NaH_2PO_4 and produce Na_2HPO_4 (weak base), again the buffer decreases change in H^+ concentration.

This buffer system is important in two sites:

1) Renal tubular fluids.
2) Inside the cell, intracellular fluid.

Because: PK of phosphate buffer= 6.8 (and PH in renal tubular fluid or inside cells is near to it because they are more acidic than ECF), and its components are concentrated in renal tubular fluid and phosphate concentration inside the cell is high.

<u>Proteins:-</u>

They are important buffers inside the cell.

Some amino acids of the proteins can dissociate into a base and H^+, so can act as buffer.
Conditions of buffer power are present, i.e., their concentration is high and their PK is near to the PH of the cell.
Example, Haemoglobin inside RBCs.($Hb^- + H^+ \leftrightarrow HHb$).
Proteins inside the cells can participate in regulation of H^+ concentration in ECF, but takes time, several hours. Because CO_2 diffusion through the cell is easy, unlike H^+ and HCO_3, which is slow.

2nd line of defence against H^+ concentration change, Respiratory system:-

Increase ▲ in H^+ concentration cause increase ▲ in pulmonary filtration and removal of excess CO_2, which will decrease ▼ H^+ concentration toward normal, and when H^+ decrease, pulmonary filtration will decrease▼, decrease CO_2 removal, which increases ▲ H^+ concentration toward normal.

3rd line of defence, Kidneys:-

Slower but stronger.
The amount of H^+ produced each day by cellular metabolism= 80mEq.
The amount of bicarbonate filtration per day= 24 X 180 = 4320 mEq/day.
(HCO_3^- conc. = 24 mEq/L, glomerular filtration rate = 180 L/day).
Reabsorption of bicarbonate is done by specific way.

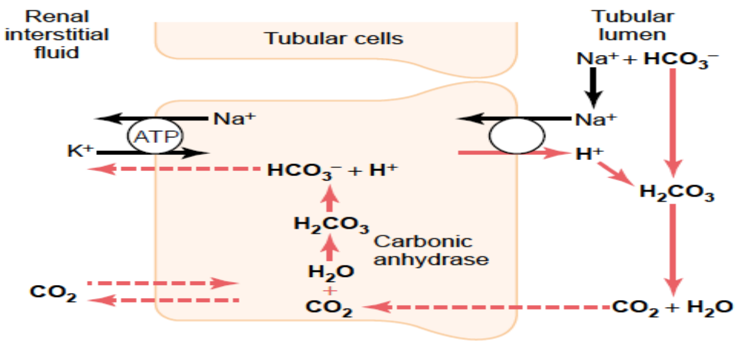

Figure 30–5

Cellular mechanisms for (1) active secretion of hydrogen ions into the renal tubule; (2) tubular reabsorption of bicarbonate ions by combination with hydrogen ions to form carbonic acid, which dissociates to form carbon dioxide and water; and (3) sodium ion reabsorption in exchange for hydrogen ions secreted. This pattern of hydrogen ion secretion occurs in the proximal tubule, the thick ascending segment of the loop of Henle, and the early distal tubule.

The amount of free hydrogen ions required for reabsorption of HCO_3^- = 4320 mEq.

Only small part of H^+ is excreted as free Hydrogen, the rest is excreted by binding with urinary buffers. Because maximum H^+ concentration in renal tubular fluid = 0.03 mEq/ L, so if all the amount of H^+ is excreted as free ions it will need 80/0.03 = 2667L of urine.

Urinary buffers such as phosphate buffer system.

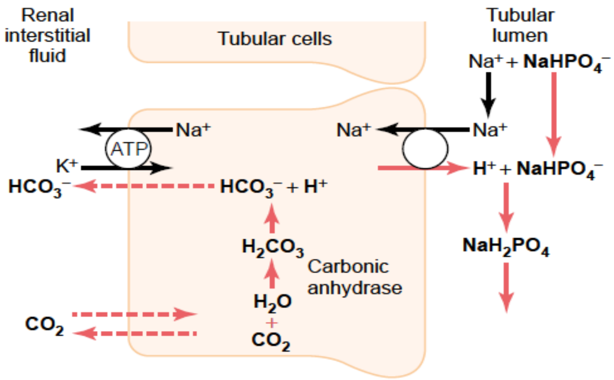

Figure 30–7

Buffering of secreted hydrogen ions by filtered phosphate ($NaHPO_4^-$). Note that a new bicarbonate ion is returned to the blood for each $NaHPO_4^-$ that reacts with a secreted hydrogen ion.

2nd Urinary buffer is Ammonia buffer system:-

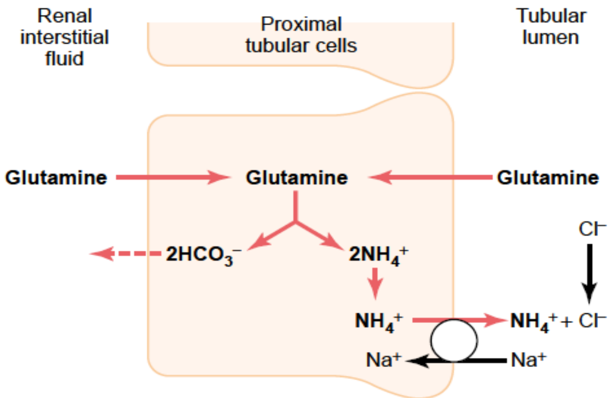

Figure 30–8

Production and secretion of ammonium ion (NH_4^+) by proximal tubular cells. Glutamine is metabolized in the cell, yielding NH_4^+ and bicarbonate. The NH_4^+ is secreted into the lumen by a sodium-NH_4^+ pump. For each glutamine molecule metabolized, two NH_4^+ are produced and secreted and two HCO_3^- are returned to the blood.

Such reaction happens in proximal tubules because of their permeability to NH_4^+.
Metabolism of glutamine, by renal glutaminase, produce glutamic acid + ammonia NH_3, and then NH_3 binds to H^+ and produce NH_4^+.
In chronic acidosis, the activity of renal glutaminase increases ▲.

The other way of ammonia buffer system, happens in collecting tubules because they are much less permeable to NH_4^+ and more permeable to NH_3, secretion of NH_3 and secretion of H^+ and then binding with Cl^- and produce NH_4Cl.

Some of the simple disorders of acid- base balance:-

Note: - partial pressure of CO_2 in arterial pressure= 40mmHg.
- Normal bicarbonate concentration = 24mEq/L.

1) Respiratory acidosis: arterial blood CO_2 will be high.

Causes: hypoventilation due to any reason, such as respiratory diseases, pneumonia, emphysema, damage in respiratory center.

2) Respiratory alkalosis: arterial blood CO_2 pressure will be low.

Causes: hyperventilation, which may be physiological hyperventilation that happens at high altitudes due to decreased▼ oxygen, or it may be happens in psychoneurotic patients.

3) Metabolic acidosis: HCO_3^- concentration will be decreased▼.

Causes:
- Renal tubular acidosis, due to secretion of H^+, HCO_3^- absorption or both.
- Chronic renal failure.
- Sever diabetes mellitus, due to a problem in glucose metabolism because cells use fatty acids instead of it as an energy source. And fatty acids metabolism produce acetoacetic acid and other acids and their accumulation can lead to acidosis.
- Sever diarrhoea, causes loss of HCO_3^-.
- Sever vomiting of intestinal content, causes loss of HCO_3^-.
- Excess ingestion of acidic drugs, for example aspirin.

4) Metabolic alkalosis: HCO^3 concentration will be increased.

Causes:
- Excess ingestion of alkaline drugs, like $NaHCO^3$.
- Vomiting of gastric content, causes loss of acids.

- Excess aldostrerone (mild metabolic alkalosis), cause increase secretion of H^+ from intercalated cells of renal tubules.
- Diuretics, most of the diuretics increase ▲ the flow of fluid in distal tubules and in this portion of tubules, absorption of Na is coupled with H^+ secretion and increased secretion of H^+ leads to metabolic alkalosis.

Table 30–3

Characteristics of Primary Acid-Base Disturbances

	pH	H^+	Pco_2	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
Respiratory acidosis	↓	↑	↑↑	↑
Respiratory alkalosis	↑	↓	↓↓	↓
Metabolic acidosis	↓	↑	↓	↓↓
Metabolic alkalosis	↑	↓	↑	↑↑

The primary event is indicated by the double arrows (↑↑ or ↓↓). Note that respiratory acid-base disorders are initiated by an increase or decrease in PCO_2, whereas metabolic disorders are initiated by an increase or decrease in HCO_3^-.

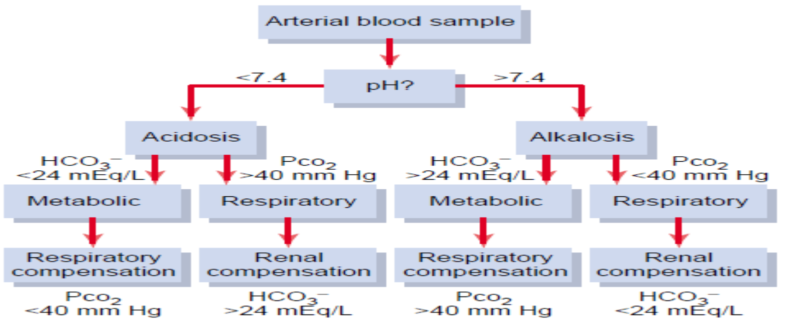

Figure 30–10

Analysis of simple acid-base disorders. If the compensatory responses are markedly different from those shown at the bottom of the figure, one should suspect a mixed acid-base disorder.

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هذه الملخصات هيمنكم. عن اجتهاد شخصي لمجموعه من طلاب الطب البشري /عدن معتمدين على عدة مصادر مما تم محاضرته او قراءته ..وقد تفيد البعض منكم. وللعلم ليس لها اية علاقة مباشره بأي عضو من اعضاء الهيئة التعليمية في الكلية. *زملائنا الأعزاء إن أصبنا فمن الله ، و إن أخطأنا فمن أنفسنا و من الشيطان " نبقى بشرا نخطئ و نصيب فلذا يرجى الإشعار في حالة وجود اي ملاحظات عبر ايميل الجروب

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